EDITORIALS

Statins in Older Adults — Evidence at Last

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For decades, one of the most important unresolved questions in preventive cardiovascular medicine has been whether statin therapy should be initiated for primary prevention in healthy older adults. Although age is among the strongest determinants of absolute risk, the benefits of statin therapy beyond 70 to 75 years of age have remained uncertain because evidence from randomized, controlled clinical trials has been sparse. This uncertainty is reflected in guidelines, in which recommendations for primary prevention become weaker for older adults.[1-3] The evidence gap has become increasingly important as populations age and cardiovascular disease occurs with increasing frequency in this age group. Notably, the uncertainty does not stem from low-density lipoprotein (LDL) cholesterol becoming less relevant as a risk factor with age. Observational studies show that the LDL cholesterol level remains strongly associated with both plaque burden and cardiovascular risk beyond 70 years of age.[4,5] What has remained unclear, however, is whether lowering the LDL cholesterol level in older adults translates into clinical benefit.

In this issue of the *Journal*, Zoungas et al.[6] report the results of the long-awaited STAREE (Statins in Reducing Events in the Elderly) trial, which fills this evidence gap. In this trial, 9971 adults 70 years of age or older without cardiovascular disease, diabetes, or dementia were randomly assigned to receive atorvastatin at a dose of 40 mg daily or placebo. The primary cardiovascular end point was a composite of death from cardiovascular causes, nonfatal myocardial infarction or stroke, or coronary revascularization, whichever occurred first. After a median follow-up of 5.9 years, treatment with atorvastatin was associated with a 30% lower risk of primary cardiovascular events than placebo (hazard ratio, 0.70; 95% confidence interval [CI], 0.61 to 0.82). The benefit was driven predominantly by nonfatal events: the risk of nonfatal myocardial infarction was approximately 42% lower with atorvastatin than with placebo, and the risk of coronary revascularization was approximately 43% lower. This effect may even be conservative; by 5 years, only 55.6% of the participants assigned to receive atorvastatin were still taking the medication, whereas open-label statin use had increased to 19.4% in the placebo group, which probably attenuated the intention-to-treat estimate.

Despite this sizeable difference in cardiovascular events, atorvastatin did not show an effect on the second primary end point, a composite of death from any cause, dementia, or persistent physical disability (hazard ratio, 0.94; 95% CI, 0.84 to 1.05). This neutral finding warrants a nuanced interpretation. More than 90% of first events were death or dementia, whereas persistent physical disability accounted for only 9%. Thus, although atorvastatin did not prolong disability-free survival, the absence of excess mortality or dementia is clinically important. These findings provide reassurance from a randomized, controlled trial that lowering LDL cholesterol levels in older adults does not adversely affect survival or cognitive health.

How, then, should the absence of a survival benefit be viewed in the context of fewer cardiovascular events? Most cardiovascular events in older adults are nonfatal. Thus, patient preferences are critical for shared decision making. Studies of health priorities suggest that the value many older adults place on avoiding nonfatal myocardial infarction, stroke, disability, and loss of independence is equal to or greater than the value placed on prolonging life itself.[7] Preventing such events may therefore represent a clinically

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meaningful benefit to older adults even when overall survival is unchanged.[8] This distinction between prolonging life and preserving health and independence is important for truly informed shared decision making.

The STAREE trial should not, however, be interpreted as a mandate to prescribe statins to everyone older than 70 years of age. Participants were healthy and independent and were selected after a placebo run-in period that required demonstration of good medication adherence. Its findings cannot automatically be extrapolated to older adults who are more frail or have multiple coexisting conditions. Cardiovascular risk varies substantially at any given age. Some older adults have extensive subclinical atherosclerosis and high absolute risk, whereas others have little or no detectable atherosclerosis and much lower risk.[9] Effective therapy therefore increases, rather than diminishes, the importance of individualized risk assessment and shared decision making.

The STAREE trial is likely to influence future prevention guidelines by strengthening the evidence base for initiating statin therapy in healthy older adults. Yet the trial results should be applied to the question that the trial addressed. The STAREE trial provides compelling evidence for the benefit and safety of initiating statin therapy in relatively healthy older adults not already receiving lipid-lowering treatment. The trial does not address whether statins can safely be discontinued in older adults who have received treatment for many years.[10] The balance between benefit, competing risks, polypharmacy, and patient priorities may differ in that setting, and dedicated evidence on deprescribing is needed. The STAREE trial, therefore, changes the central clinical question. It is no longer whether statins can prevent cardiovascular events when initiated in healthy older adults, but whom to treat to achieve meaningful absolute benefit. The trial tells us that it is not too late to start statin therapy. Whether there comes a time when it is safe to stop after years of treatment remains unanswered.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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1. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2021;42:3227-337.
2. Blumenthal RS, Morris PB, Gaudino M, et al. 2026 ACC/AHA/AACVPR/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of dyslipidemia: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. J Am Coll Cardiol 2026;87:2624-757.
3. Mortensen MB, Falk E. Primary prevention with statin in the elderly. J Am Coll Cardiol 2018;71:85-94.
4. Mortensen MB, Nordestgaard BG. Elevated LDL cholesterol and increased risk of myocardial infarction and atherosclerotic cardiovascular disease in individuals aged 70-100 years: a contemporary primary prevention cohort. Lancet 2020;396:1644-52.
5. Andersen MH, Jensen JM, Kanstrup H, et al. Low-density lipoprotein cholesterol, coronary plaque burden, and myocardial infarction in adults aged 76-92 years: the Western Denmark Heart Registry. Eur J Prev Cardiol 2026 February 16 (Epub ahead of print).
6. Zoungas S, Wolfe R, Moran C, et al. Atorvastatin, cardiovascular events, and disability-free survival in older adults. N Engl J Med 2026;395:1259-72.
7. Stolker JM, Spertus JA, Cohen DJ, et al. Rethinking composite end points in clinical trials: insights from patients and trialists. Circulation 2014;130:1254-61.
8. Armstrong PW, Westerhout CM. Composite end points in clinical research: a time for reappraisal. Circulation 2017;135:2299-307.
9. Mortensen MB, Fuster V, Muntendam P, et al. Negative risk markers for cardiovascular events in the elderly. J Am Coll Cardiol 2019;74:1-11.
10. Bonnet F, Poulizac P, Rousselot N, et al. Discontinuation of statins for primary prevention of atherosclerotic cardiovascular disease in adults aged 75 years or older (SAGA/SITE): a multicentre, open-label, pragmatic, non-inferiority randomised trial. Lancet Healthy Longev 2026;7:100884.

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Obexelimab and the Promise of Nondepleting B-Cell Therapy in IgG4-Related Disease

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IgG4-related disease has emerged as one of the clearest human models for understanding the role of B-lineage cells in immune-mediated inflammation. Although glucocorticoids remain effective for inducing remission, relapse during tapering is common, cumulative toxic effects are substantial, and durable disease control remains difficult to achieve. Della-Torre et al.[1] now report in the *Journal* the findings of the INDIGO trial. This phase 3 INDIGO trial of obexelimab is notable,

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